

WHAT IS CLAIMED IS:

1. A method of inhibiting CD28 pathway activation associated with an increase in cellular production of a T_H CD28 lymphokine in a T cell population, wherein activation occurs by the binding of a stimulatory CD28 ligand to a CD28 receptor stimulatory binding site, the method comprising the steps of:
 - 5 a) selecting an inhibitory ligand capable of binding to the stimulatory CD28 ligand;
 - b) providing the inhibitory ligand in a biologically compatible form; and
 - 10 c) administering the inhibitory ligand to the population in an amount sufficient to bind and inhibit the stimulatory ligand from binding the CD28 receptor stimulatory binding site.
2. The method of Claim 1, wherein the stimulatory ligand comprises a natural CD28 ligand.
- 15 3. The method of Claim 1, wherein the inhibitory ligand comprises an antibody or fragment thereof to the stimulatory ligand.
4. The method of Claim 1, wherein the inhibitory ligand comprises a soluble form of CTLA-4.
- 20 5. The method of Claim 4, wherein the ligand comprises CTLA-4Ig.
6. The method of Claim 1, wherein the inhibitory ligand is of synthetic origin.
- 25 7. The method of Claim 1, wherein the inhibitory ligand comprises a recombinant molecule.
8. The method of Claim 1, further comprising the step of:
 - 30 d) administering a second inhibitory ligand capable of binding but not stimulating the CD28 receptor binding site.

9. A method of suppressing the production of a T_H CD28 lymphokine by a population of T cells, the method comprising the steps of:

- a) administering an inhibitory ligand which binds a stimulatory ligand for CD28;
- 5 b) providing the ligand in biologically compatible form; and
- c) administering the provided ligand in an amount sufficient to suppress production of the lymphokine in the population.

10 10. The method of Claim 9, wherein the inhibitory ligand comprises a soluble form of CTLA-4.

11. The method of Claim 10, wherein the inhibitory ligand comprises CTLA-4Ig.

15 12. The method of Claim 9, wherein the T cell population is in a patient in an autoimmune state.

13. A method of suppressing T_HCD28 lymphokine production in a patient having a population of T cells, the method comprising the steps of:

- a) providing an inhibitory ligand which binds a natural stimulatory
5 ligand for CD28; and
- b) administering the inhibitory ligand in a therapeutically effective amount to the population of T cells.

14. The method of Claim 13, wherein the administration of the ligand
10 to the population of T cells is *in vivo*.

15. The method of Claim 13, wherein the administration of the ligand to the population of T cells is *in vitro*, and further comprising the step of:

- d) introducing the population of T cells into the patient after
15 administration.

16. The method of Claim 15, wherein the T cell population is removed from the patient prior to ligand administration.

20 17. The method of Claim 13, wherein the inhibitory ligand comprises a soluble form of CTLA-4.

18. The method of Claim 17, wherein the inhibitory ligand comprises CTLA-4Ig.

19. A method of treating an autoimmune disease in a patient comprising the steps of:

- a) selecting an inhibitory ligand which binds a natural stimulatory ligand to CD28; and
- 5 b) administering a therapeutically effective amount of the ligand to the patient.

20. The method of Claim 19, wherein the stimulatory ligand is B7 and the inhibitory ligand comprises a soluble form of CTLA-4.

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21. The method of Claim 19, wherein the inhibitory ligand comprises CTLA-4Ig.

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22. The method of Claim 20, wherein the administration is *in vivo*.

23. The method of Claim 20, wherein the administration is *in vitro* to a population of cells removed from the patient, and further comprising the step of:

- c) reintroducing the cells to the patient after administration.

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24. The method of Claim 20, wherein the autoimmune disease is multiple sclerosis.

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